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16. ABSTRACT

The processes which govern the accumulation of lipophilic toxicants in animal tissues are equilibrium processes (partictioning) and kinetic processes. Kinetic processes include diffusion, transport by body fluids, and biodegradation. If biodegradation and transport by body fluids is negligible, then (at constant temperature, pressue, and viscosity) the transport of a solute between two points in a tissue is determined solely by the concentration gradient. The diffusion of a lipophilic toxicant within a tissue, consisting of millions of cells, may be viewed as if the tissue were a homogenous and isotropic system. Physical contact between membranes is required in order for diffusional exchange of lipophilic substances to occur. If molecular transport of a lipophilic toxicant in isolated tissues is truly a difusion process, then it should be possible to describe the process in terms of mathematical equations commonly used to describe the conduction of heat in homogenous and isotropic solids. The present approach compares well with other more direct and empirical methods for estimating diffusivity and it has the advantage that diffusivity so calculated in biologically realistic. The ability to evaluate toxicant uptake by organs of various sizes is theoretically factored in the method. Likewise, the physiological characteristics as a whole are factored by using the empirical data directly consistent with the stated theoretical framework.

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Estimation of Molecular Diffusivity in Isolated Animal Tissues

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The processes which govern the accumulation of lipophilic toxicants in animal tissues are equilibrium processes (partitioning) and kinetic processes (Lakowicz, Hogan & Omann, 1977). Kinetic processes include diffusion, transport by body fluids, and biodegradation. If biodegradation and transport by body fluids is negligible, then (at constant temperature, pressure, and viscosity) the transport of a solute between two points in a tissue is determined solely by the concentration gradient.

The diffusion of a lipophilic toxicant within a tissue, consisting of millions of cells, may be viewed as if the tissue were a homogenous and isotropic system. Physical contact between membranes is required in order for diffusional exchange of lipophilic substances to occur (Lenard & Rottman, 1976). Diffusion will continue until the surface concentration and the concentration at the center of the tissue are the same. It is the rapid initial rise of concentration in the surface tissue layer that is the "driving force" for the flow of the toxicant into the tissue. In bivalve mollusks the enzyme systems required for the degradation of lipophilic toxicants are either absent or present in very low concentrations (Lee, Sauerheber & Benson, 1972). Therefore, in isolated tissues from oysters (or any other bivalves) the transport of lipophilic toxicants into the tissue should be solely by diffusion.

If molecular transport of a lipophilic toxicant, in isolated tissues, is truly a diffusion process, then it should be possible to describe the process in terms of mathematical equations commonly used to describe the conduction of heat in homogenous and isotropic solids. The geometry of the isolated "body" tissue from oysters (Riley *et al.*, 1981) closely approximates a sphere. Therefore, the mathematical solution for diffusion in a sphere can be used with appropriate initial and boundary conditions to calculate the molecular diffusivity in whole tissues. The partial differential equation

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which describes diffusion in the body is:

$$\frac{\partial v}{\partial t} = D\left(\frac{\partial^2 v}{\partial r^2} + \frac{2}{r}\frac{\partial v}{\partial r}\right) \tag{1}$$

where v is the tissue concentration divided by the ambient water concentration, t is the time (sec), r is the distance of the boundary from the center of the tissue (cm), a is the radius of the tissue calculated by assuming that the ratio of wet weight to tissue volume is 1·0 (cm), and D is the molecular diffusivity ($cm^2\ sec^{-1}$).

The initial and boundary conditions for equation (1) are that at $t = 0$, $v = 0$, and at $r = a$, $v = V$. V is the concentration in the surface tissue layer divided by the ambient water concentration. It is assumed that the magnitude of V in the surface tissue layer is the same as the maximum concentration ratio. Also, it is assumed that maximum concentration ratio in the surface tissue layer is attained in a very short time compared to the time required for transport to the center of the tissue. The solution which satisfies the above initial and boundary conditions is (Carslaw & Jaeger, 1960):

$$v_{av}V^{-1} = 1 - 6\pi^{-2}\sum_{n=1}^{\infty} n^{-2}\, e^{(-Fn^2\pi^2)} \tag{2}$$

where v_{av} is the average tissue concentration and F is a dimensionless time better known as a Fourier number and defined as:

$$F = Dta^{-2}. \tag{3}$$

Utilizing equations (2) and (3), D can be estimated for naphthalene from the data summarized in Table 1. The value of $v_{av}V^{-1}$ was calculated for each datum and the corresponding Fourier number

TABLE 1

Range of observations used to calculate the molecular diffusivity[a]

Experiment	a (cm)	t (sec)	$v_{av}V^{-1}$
1 $n = 20$	0·18 to 0·26	3×10^2 to 9×10^3	0·05 to 0·51
2 $n = 12$	0·20 to 0·35	$5{\cdot}4\times10^4$ to $2{\cdot}6\times10^5$	0·64 to 1·06[b]

[a] The range of observations for experiment 1 are from unpublished data, and the data for experiment 2 are calculated from the data derived from Riley *et al* (1981), their Table 3.

[b] $v_{av}V^{-1}$ was calculated utilizing an assumed value for V of 60. This value was the mean value for all 72 hr bioaccumulation factors from Riley *et al.* (1981), their Tables 2 and 3.

was calculated for various assumed values of D (equation (3)). All the data were plotted for each assumed value of D and each plot was compared to the general solution from equation (2). The best estimate of D was determined by visual comparison of the plotted data to the general solution (Fig. 1). The best fit was obtained using a value for D of 8×10^{-8} cm^2 sec^{-1}.

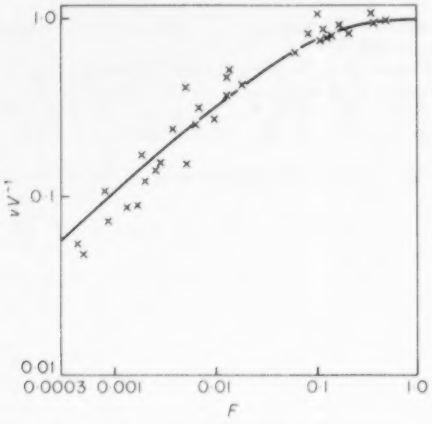

FIG. 1. The general solution for equation (2) (solid line) and the plotted values of $v_{av}V^{-1}$ and corresponding F values calculated from equation (3) utilizing a value for molecular diffusivity of 8×10^{-8} cm^2 sec^{-1}.

This value is reasonable when compared to the magnitude of D for other compounds with regards to lateral diffusion in lipid membrane systems. For example, $D = 5{\cdot}7\times10^{-7}$ cm^2 sec^{-1} at 37°C for the pesticide lindane in an artificial bilayer as determined by a fluorescence quenching technique (Lakowicz *et al.*, 1977); $D = 6\times10^{-8}$ cm^2 sec^{-1} at 37°C for lateral diffusion of phospholipids in sarcoplasmic-reticulum vesicles determined by a spin labeling technique (Scandella, Devaux & McDonnell, 1972); $D = \cong 2\times10^{-7}$ cm^2 sec^{-1} at 25°C for lipids in artificial bilayers as determined by fluorescence correlation spectroscopy (Fahey *et al.*, 1976).

The present approach compares well with other more direct and empirical methods for estimating diffusivity and it has the advantage that diffusivity so calculated is biologically realistic. The ability to evaluate toxicant uptake by organs of various sizes is theoretically factored in the method. Likewise, the physiological characteristics as a whole are factored by using the empirical data directly consistent with the stated theoretical framework.

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